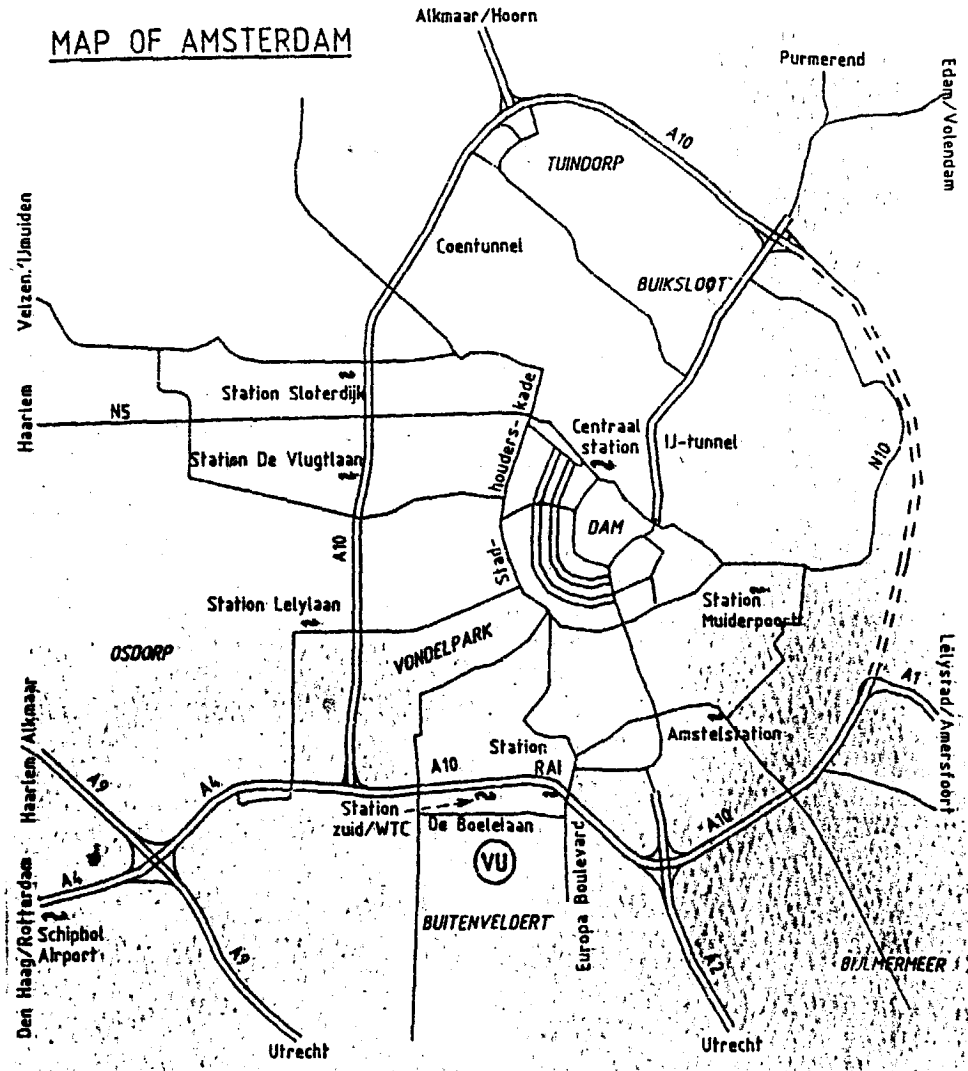
MAP OF AMSTERDAM



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Third International ISSX

1991 ISSX AMSTERDAM

drug metabolism: molecules, models and man

24-28 June 1991 Amsterdam The Netherlands

PROGRAMME

Organizing committee

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0031-20-5482963

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Welcome to the 3rd International ISSX Meeting on D... Molecules, Models and Man

On behalf of the Board of the Vrije Universiteit I am very plea... at the 3rd International ISSX Meeting on Drug Metabolism: Mo...
As I understand, ISSX stands for a relatively young, but v... International Society for the Study of Xenobiotics, an internationa... together all those interested in the various aspects of xenobiotics, regard... they are drugs, pesticides, industrial chemicals or environmental contaminants. ... interesting to notice that the first time this International ISSX Meeting is organized in... Europe, the Netherlands, notably in Amsterdam, are host of the Meeting.

Apart from its economic role in this region of Europe, Amsterdam, the largest city of this small European country, is known for its historical, architectural, cultural and social qualities and achievements. I sincerely hope you will take the opportunity to enjoy the hospitality and the atmosphere the Netherlands in general and Amsterdam in particular can offer you.

The Vrije Universiteit (Free University) is a private university. Over a century ago, in 1880, under the leadership of the theologian and statesman Dr. Abraham Kuyper, orthodox protestant Dutchmen established an association, the goal of which was the foundation of a Free Christian University. 'Free' here means free from church and state, bound only by the Word of God. Its establishment provided an answer to the discrimination experienced in many areas of society, including that of higher education. Presently, the Vrije Universiteit comprises 15 faculties, 1,800 lecturers, 300 professors, 1,700 non-academic staff and teaching facilities for 12,000 students.

Our University is glad to extend you hospitality for the 3rd International ISSX Meeting, not only because we can offer good conference facilities, but also because it strengthens our belief that research and education in chemical, pharmaceutical, biological and medical sciences is of utmost importance for the well-being of mankind and our environment.
I wish you an exciting meeting and a pleasant stay in Amsterdam.

Welcome to the Vrije Universiteit,

Prof. Dr. C. Datema
Rector Magnificus Vrije Universiteit Amsterdam

Vo Proceedings available

General information

Language Conference language is English

Lunch Lunches for participants are available without extra charge every day between 12.30 - 14.00

Coffee Coffee and tea will be available free of charge during the breaks at different locations

Banking facilities Banking facilities are available at the Congress site

Technical equipment The following technical aids are available
- slide single projection (5 x 5 cm)
- overhead

Speakers are kindly requested to hand in and check their slides before the beginning of their session.

Conference Venue
De Boelelaan 1105
1081 HV AMSTERDAM, The Netherlands
Tel. +31 20 548 4982/4983 (only during the conference)

All lecture halls, and the exhibition are located in the Main Building of the Free University (Vrije Universiteit)
(see map on p. 45)

An information and registration desk will be open daily starting Monday from 09.00 a.m. till 30 minutes after the close of the sessions.

Conference Office
Conference Service Free University

Ms M. van Urk
De Boelelaan 1105, 1081 HV AMSTERDAM
P.O. Box 7161, 1007 MC AMSTERDAM
The Netherlands

Tel. + 31 20 548 4656
Fax + 31 20 646 2425

Programme - summary

Monday 24 June 1991	Registration for Course	09.00 - 11.00
	Course 1 and Course 2	10.30 - 17.00
	Registration	11.00 - 20.00
	Opening Keynote lecture	20.00 - 21.00
	Get together	21.00 - 22.30
Tuesday 25 June 1991	Session 1 (Plenary)	09.00 - 12.30
	Poster session 1	13.30 - 15.00
	Sessions 2-4 (Parallel)	15.00 - 17.00
	Boat trip and welcoming reception	17.30 - 20.00
Wednesday 26 June 1991	Session 5 (Plenary)	09.00 - 12.30
	Poster session 2	13.30 - 15.00
	Sessions 6-8 (Parallel)	15.00 - 17.00
	Cytochome P450 debate	17.00 - 18.30
Thursday 27 June 1991	Session 9 (Plenary)	09.00 - 12.30
	ISSX Business meeting	13.30 - 14.30
	Conference dinner	19.00 - 23.00
Friday 28 June 1991	Session 10 (Plenary)	09.00 - 12.30
	Sessions 11-13 (Parallel)	13.30 - 15.30
	Closing	15.30

Participants presenting a poster are requested to put their posters up between 08.00 - 09.00 hours, and take them down between 16.00 and 17.00 hours. They need to be present at their posters from 13.30 - 15.00.

Monday, 24 June 1991

Registration courses 09.00 - 11.00

Course 1 10.30 - 17.30 Room 5A - 05 Organizers

Drug metabolism and pharmacokinetics regulatory guidelines for the registration of pharmaceutical products - theory and practice	David E. Case and Committee on Registration Affairs of the ISSX
a. Introduction to international regulatory guidelines	D.E. Case, ICI Pharmaceuticals, UK
b. The guidelines in Europe	A. Bell, Glaxo Group Research, UK
c. The guidelines in America	J.G. Dent, Smith Kline Beecham Pharmaceuticals, USA)
Lunch	
d. The guidelines in Japan	H. Shindo, Sankyo Co., Ltd., Japan
e. Panel forum queries and discussion	Chair M. van der Waart, Organon, The Netherlands
f. Concluding remarks	

Course 2 10.00 - 17.15 Room 6A - 05 Organizers

Computers in drug disposition studies	Nico P.E. Vermeulen and Peter J. van Bladeren
a. Computer-aided prediction of biotransformation reactions and toxicity	F. Darvas, Compudrug Ltd., Budapest, H
b. Computer graphics/molecular modeling in receptor- and active site mapping	G. Donné-Op den Kelder, Free University Amsterdam, NL
c. QSAR-approaches in toxicology	J.L.M. Hermens, University of Utrecht, NL
Lunch	

d. Physiologically based pharmacokinetic modeling and bioactivation of xenobiotics	H. Clewell , Wright - Patterson Airforce Base, USA
e. Pattern recognition analysis and body fluid profiling	J. van der Greef, TNO Biotechnology and Chemistry Institute, Zeist, NL
f. Concluding remarks	

Evening

18.00 - 20.00	Registration and coffee

Aula

20.00	Welcome by Gerard J. Mulder Chairman of the Organizing Committee
20.05	Opening of the meeting by Professor E.H. Burger Vice Rector of the Free University of Amsterdam
20.15	Keynote lecture "New vistas in xenobiotic metabolism in vivo and in vitro" by Franz Oesch, President of ISSX (Mainz, Germany)
21.00 - 22.30	Get together

Tuesday, 25 June 1991 09.00 - 12.30

Session 1 ***Drug Metabolism in Man***

Aula

Chair R.W. Estabrook, USA
Co-chair G.J. Mulder, NL

09.00 - 09.05	Chairman's introduction	
09.05 - 09.40	a. Oxidative metabolism *in vivo*	D.D. Breimer, Leiden, NL
09.40 - 10.15	b. Cytochrome P450 in man	J. Miners, Bedford Park, AUS
10.15 - 10.50	c. Conjugative metabolism *in vivo*	R. Verbeeck, Brussels, B
10.50 - 11.20	Coffee break	
11.20 - 11.55	d. Glutathione transferases in man	D.J. Harrison, Edinburgh, UK
11.55 - 12.30	e. N-Acetyltransferases in man	U.A. Meyer, Basel, CH

13.30 - 15.00 Poster session I (1 - 5)

1 Drug metabolism in man

A. In vivo studies (1-16)
B. Enzymes in vitro (1-24)
C. Clinical Pharmacology (1-4)

2 Drug metabolism in animals in vivo

A. Metabolic profiling (1-29)
B. Sex differences, stereoselectivity protein binding and other factors (1-17)

3 Diet and intestinal drug metabolism (1-2)

4 Analytical methods in drug metabolism (1-5)

5 Mechanisms of toxicity in vivo and in vitro (1-25)

15.00 - 17.00 Parallel sessions 2-4

Session 2 ***Species and Sex Differences From Animal to man***

Room: KC - 07

Chair R. Kato, Jpn.
Co-chair J.J.P. Heijkants, B

15.00 - 15.30	a. Species differences	J. Caldwell, London, UK
15.30 - 16.00	b. Sex differences	Y. Yamazoe, Tokyo, Jpn
16.00 - 16.30	c. Species differences in protein binding	F. Belpaire, Gent, B
16.30 - 16.45	d. Stereochemical aspects of the disposition of indobufen in rats, mice and human subjects	N. Grubb, et al., London, UK
16.45 - 17.00	e. The metabolism and excretion of risperidone in rats, dogs and man	W. Meuldermans, et al., Beerse, B

Session 3 ***Food and Drug Metabolism***

Room 8A - 05

Chair C.D. Klaassen, USA
Co-chair J. Noordhoek, NL

15.00 - 15.30	a. Food constituents and intestinal microbial drug metabolism	I. Rowland, Carshalton, UK
15.30 - 16.00	b. Modulation of xenobiotic metabolism by diet and nutrition	C.S. Yang, Piscataway, USA
16.00 - 16.30	c. Disposition of BHA and BHT in animals and man	H. Verhagen, Zeist, NL
16.30 - 16.45	d. Intestinal metabolism of Saccharomyces boulardii a model oral biotherapeutic agent	S.M. Sanins, et al., Seattle, WA, USA
16.45 - 17.00	e. Lactational transfer of a low dose of TCB and HCB induces cytochrome P-450IVA1 in neonates. Evidence for a synergistic mechanism	J.T. Borlakoglu et al., Strasbourg, F

Session 4 ***Analytical Techniques and Approaches***

Room: 8A - 00

Chair T.A. Baillie, USA
Co-chair J.M. te Koppele, NL

15.00 - 15.30	a. Mass spectroscopy and pattern recognition	J. Van der Greef, Zeist, NL
15.30 - 16.00	b. Trends in HPLC	U.A.Th. Brinkman, Amsterdam, NL
16.00 - 16.30	c. Analysis of conjugates	L.P.C. Delbressine, Oss, NL
16.30 - 16.45	d. Evidence for complex formation between rabbit lung flavin-containing monooxygenase and calreticulin	J.R. Cashman, et al. San Francisco, CA, USA
16.45 - 17.00	e. Sensitive analytical method for a drug and its metabolites using a bioimage analyzer - diazepam and its metabolites in pregnant and fetal rats	S.I. Nagatsuka, et al. Ibaraki-ken, Japan
17.30 - 20.00	Welcoming Reception	

Wednesday, 26 June 1991 09.00 - 12.30

Session 5 ***Molecular Mechanisms and Toxicology***

Aula

Chair P. Moldeus, S
Co-chair N.P.E. Vermeulen, NL

09.00 - 09.05	Chairman's introduction	
09.05 - 09.40	a. Bioactivation and toxicity I.	T.A. Baillie, Seattle, USA
09.40 - 10.15	b. Bioactivation and toxicity II.	F.P. Guengerich, Nashville, USA
10.15 - 10.50	c. Bioactivation and physiological modelling	H.J. Clewell III, Wright-Patterson Airforce base, USA
10.50 - 11.20	Coffee break	
11.20 - 11.55	d. Free radicals effects and protection mechanisms	A. Bast, Amsterdam, NL
11.55 - 12.30	e. Mechanism-based hazard assessment	D. Henschler, Würzburg, FRG

13.30 - 15.00 Poster session II (6A - 13A)

6 **Drug metabolizing enzymes in vitro**

- A. Cytochrome P450 and flavin monoxygenases (1-19)
- B. Other enzymes (1-16)
- C Induction of drug metabolizing enzymes (1-15)
- D. Mechanisms of biotransformation enzymes (1-14)

7 **Idiosyncratic reactions and reactive intermediates (1-4)**

8 **Intact cell preparations in vitro**

- A. Engineered cells and cell lines (1-7)
- B Isolated cell systems and liver perfusion (1-21)

9 **Transport, excretion of drugs and bio-pharmaceutical aspects (1-14)**

11 Metabolism of peptides and proteins (1-5)

12 Carcinogens and biomonitoring (1-14)

13 Metabolism of metal-containing drugs and metal ions (1-4)

15.00 - 17.00 Parallel sessions 6-8

Session 6 *Enzyme Mechanisms Active Sites and SAR*

Room: KC - 07

Chair A.Y.H. Lu, USA
Co-chair P.J. van Bladeren, NL

15.00 - 15.30	a. Cytochrome P450	P.R. Ortiz de Montellano, San Francisco, USA
15.30 - 16.00	b. Conjugating enzymes	R.N. Armstrong, College Park, USA
16.00 - 16.30	c. Active site-directed inhibition	W.L. Alworth, New Orleans, USA
16.30 - 16.45	d. Characterization of molecular species of liver microsomal carboxylesterases of several animal species and humans	T. Satoh, et al. Chiba, Japan
16.45 - 17.00	e. Renal and hepatic structure-activity studies with rat and bovine C-S lyase enzymes	A.J. Wilson, et al. Nottingham, UK

Session 7 *Idiosyncratic Reactions*

Room: 1A - 05

Chair J. Uetrecht, Can
Co-chair H. Nieuwenhuyse, NL

15.00 - 15.30	a. Idiosyncratic allergic hepatitis	L.R. Pohl, Bethesda, USA
15.30 - 16.00	b. Testing of idiosyncratic drug reactions	B.K. Park, Liverpool, UK
16.00 - 16.30	c. Mechanisms	D.Mansuy, Paris, F
16.30 - 16.45	d. Interaction of diflunisal acyl glucuronide and its isomers with albumin	R.G. Dickinson, et al. Brisbane, AUS
16.45 - 17.00	e. Possible role of free radical formation in clozapine induced agranulocytosis	V. Fischer, et al. Basel, CH

Session 8 *In Vitro Biotransformations Models*

Room: 2A - 00

Chair F. Oesch, D
Co-chair B. Blaauboer, NL

15.00 - 15.30	a. Hepatocytes as biotransformation model	V. Rogiers, Brussels, B
15.30 - 16.00	b. Genetically engineered V79 cells for drug metabolism studies	J. Doehmer, Mainz, FRG
16.00 - 16.30	c. Transgenic animals	W.R. Beltz, Boston, USA
16.30 - 16.45	d. Bacterial expression of spectrally active rat cytochrome P-450 2G1 (P-450 olf)	A. Kempf, et al. Basel, CH
16.45 - 17.00	e. Xenobiotic metabolising activity of human and rat epidermal keratinocyte cultures	P. Nasseri-Sina, et al. London, UK

17.00 - 18.30 *Debate: "Does induction of CYP1A1 indicate potential carcinogenicity?"*
Aula

Introduction of participants, rules of order	R.W. Estabrook, Dallas,TX,USA
Statement of the problem, industries dilemma	D. Case, Cheshire, UK
Opening arguments pro	D. Parke, Guildford, UK
	P. Maurel, Montpellier, F
contra	A. Parkinson, Kansas City, USA
	J. Caldwell, London, UK
Rebuttals pro and contra	
Unanswered questions from the audience	
Summary	R.W. Estabrook, Dallas,TX,USA

Thursday, 27 June 1991 09.00 - 12.30

Session 9 ***Transport of Xenobiotics and Metabolites***
Aula
Chair R.L. Smith, UK
Co-chair D.D. Breimer, NL

09.00 - 09.05	Chairman's introduction	
09.05 - 09.40	a. Hepatic transport mechanisms	D.K.F. Meijer, Groningen, NL
09.40 - 10.15	b. Transport mechanisms in the kidney	M.E. de Broe, Antwerpen, B
10.15 - 10.50	c. Transport mechanisms in the skin	F. Teeuwes, Palo Alto, USA
10.50 - 11.20	Coffee break	
11.20 - 11.55	d. Pulmonary uptake systems	G.M. Cohen, London, UK
11.55 - 12.30	e. Binding to blood components	J.P. Tillement, Paris, F

13.30 - 14.30 ISSX Business meeting Room Aula

Afternoon

Free

19.00 - 23.00 Conference dinner, Breughelhuys, Smaksteeg 20, Amsterdam
(next to the Sonesta Hotel)

Friday, 28 June 1991 09.00 - 12.30

Session 10 *Xenobiotics and the Environment*

Aula

Chair D. Henschler, D
Co-chair J.L.M. Hermens, NL

09.00 - 09.05	Chairman's introduction	
09.05 - 09.40	a. Metabolism of xenobiotics in the environment dioxins	H. Poiger, Schwerzenbach, CH
09.40 - 10.15	b. Halogenated aromatic compounds as P450 inducers	S.H. Safe, College Station, USA
10.15 - 10.50	c. Microbial metabolism in the environment	A. Zehnder, Wageningen, NL
10.50 - 11.20	Coffe break	
11.20 - 11.55	d. Biotransformation in invertebrates and plants	D.H. Hutson, Sittingbourne, UK
11.55 - 12.30	e. Fate of xenobiotics in soil	T.R. Roberts, Harrogate, UK

13.30 - 15.30 Parallel sessions 11-13

Session 11 *Disposition of Protein and Peptides*

Room 14A - 00

Chair M. Cayen, USA
Co-chair M. van der Graaff, NL

13.30 - 14.00	a. Safety evaluation of recombinant proteins	K.B. Seamon, Bethesda, USA
14.00 - 14.30	b. Peptide metabolism	J. Sandow, Frankfurt/Mainz, FRG
14.30 - 15.00	c. Peptide transport	J. Verhoef, Leiden, NL
15.00 - 15.15	d. Determination of rates of hydrolysis of vasopressin analogs by digestive proteases using an immobilized digestive enzyme assay	R.B. van Breemen, et al. Raleigh, NC, USA
15.15 - 15.30	e. The disposition of ICI 118630 in animals and man	A. Warrander, et al. Macclesfield, UK

Session 12 *Biotransformation and Biomonitoring*

Room: KC - 07

Chair T. Green, UK
Co-chair J. Meerman, NL

13.30 - 14.00	a. Hemoglobin and DNA adducts	P.B. Farmer, Carshalton, Surrey, UK
14.00 - 14.30	b. Mercapturates as tools in biomonitoring	N.P.E. Vermeulen, Amsterdam, NL
14.30 - 15.00	c. Biomonitoring of industrial chemical and agrochemicals	N.J. van Sittert, The Hague, NL
15.00 - 15.15	d. Adducts of ethylene oxide and vinyl chloride as indicators of exposure	H.M. Bolt, et al. Dortmund, D
15.15 - 15.30	e. Genotoxicity and DNA-binding of neurotoxic organophosphates	A. Mentzschel, et al. Würzburg, D

Session 13 *Disposition of Metals and Metal-containing Drugs*

Room: 8A - 05

Chair J. Miners, Aus
Co-chair A. Bast, NL

13.30 - 14.00	a. Disposition of cadmium	C.D. Klaassen, Kansas City, USA
14.00 - 14.30	b. Disposition of platinum drugs	L.R. Kelland, Belmont/Sutton,UK
14.30 - 15.00	c. Disposition of organotin compounds	A.H. Penninks, Zeist, NL
15.00 - 15.15	d. Cadmium accumulation after dietary administration of $CdCl_2$ or Cd-metallothionein in rats and the effects of mineral supplements	J.P. Groten, et al. Zeist, NL
15.15 - 15.30	e. Biooxidation of gold (I) to gold (III) detected by T memory cells	E. Gleichmann, Düsseldorf, D

15.30 Closing of the meeting Aula

1. Drug Metabolism in Man (In vivo studies) (1A1 - 1A19)

1A9 Morphine kinetics after diamorphine infusion in premature neonates.
Barrett David A., Alun C. Elias Jones*, Nicholas Rutter*, P. Nicholas Shaw and Stanley S. Davis
Dept. of Pharmaceutical Sciences and *Dept. of Child Health, Nottingham University, Nottingham, UK.

1A14 Pharmacokinetics of piroximone in patients with chronic liver disease.
Bortakoglu Jürgen T., Gabrielle Cremer, Anne-Marie Joder-Ohlenbusch and Klaus D. Haegele
Marion Merrell Dow, Strasbourg, France.

1A10 The effects of food on the bioavailability and the disposition of single oral doses of piroximone, a new cardiotonic agent.
Bortakoglu Jürgen T., Gabrielle Cremer, Anne-Marie Joder-Ohlenbusch and Klaus D. Haegele
Marion Merrell Dow, Strasbourg, France.

1A6 Effect of multiple rifabutin administration on isoniazid pharmacokinetics and metabolism in healthy volunteers.
Breda M.^, E. Pianezzola^, M. Strolin-Benedetti^, C. Efthymiopoulos^, M. Carpentieri^, P. Olliaro^ and R. Rimoldi°
^ Farmitalia Carlo Erba, R&D-Erbamont Group, Milan, Italy.
° Ospedale di Circolo, Varese, Italy.

1A5 Absorption and disposition of the anti-inflammatory drug flosulide (CGP 28 238) in one healthy male volunteer.
Gschwind H.P., P.G. Ferrini, A. Sioufi*, F. **Waldmeier** and C. Czendlik
CIBA-GEIGY Ltd., Pharma R&D Dept., K-136.283, CH-4002 Basel, Switzerland; * CIBA-GEIGY SA, Centre de Recherche Biopharmaceutique, Rueil-Malmaison, France.

1A8 Polymorphic N-acetyltransferase: a comparison of phenotype and genotype.
Hickman D. and E. Sim
University Department of Pharmacology, South Parks Road, Oxford OX1 3QT, UK.

1A20 Metabolic disposition of 14C-CI-943 in man.
Hoffmann G., W. Klemisch, A. v. Hodenberg, U. Bayer, K.-O. Vollmer and T. Kronbach
Goedecke Research Institute,
Dept. of Pharmacokinetics and Metabolism, Mooswaldallee 1-9, D-7800 Freiburg, FRG.

1A19 Fluconazole: metabolic stability and renal clearance lead to predictability of pharmacokinetics in man.
Jezequel S.G.
Dept. of Drug Metabolism, Pfizer Central Research, Sandwich, Kent, UK.

1A17 Structural characterization of pantoprazole urinary, fecal and plasma metabolites after single dose oral or intravenous administration to human volunteers.
Kuo G.Y., T.J. Blake, K.M. Anderson, J. Kao, M. Carbonaro, C. Broom*, E. Sturm**, R. Huber**, B. Kohl** and D.M. Dulik
Dept. of Drug Metabolism, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406, USA; * Dept. of Clinical Pharmacology, SmithKline Beecham Pharmaceuticals, Welwyn, Herts., UK; ** Research Laboratories, Byk Gulden, Konstanze, FRG.

1A7 Debrisoquine-type oxidation metabolic phenotype in diabetic patients.
Lam Y.W. Francis, Daniel T. Casto and James F. Dunn
Depts. of Pharmacology, Pediatrics, and Medicine, The University of Texas Health Science Center at San Antonio; and The College of Pharmacy, University of Texas at Austin, TX, USA.

1A13 Haloperidol interconversion variabilities and the RH/HL ratio in schizophrenic patients.
Lam Y.W. Francis, W.H. Chang, M.W. Jann and H. Chen
Dept. of Pharmacology, University of Texas Health Science Center at San Antonio, TX, USA; Taipei Psychiatric Ctr. Taipei;
Dept. Pharmacy Practice, School of Pharmacy, Mercer University, Atlanta, GA, USA.

1A3 N^+-glucuronidation of aliphatic tertiary amines, a general phenomenon in the metabolism of H1 antihistamines in humans.
Luo H., **E.M. Hawes**, G. McKay, E.D. Korchinski and K.K. Midhua
Colleges of Pharmacy and Medicine, University of Saskatchewan, Saskatchewan, Canada S7N 0W0.

1A18 Metabolic fate of 14C-FOY-305 in man, rat and dog.
Midgley I., A.J. Hood, P. Proctor, L.F. Chasseaud, S.R. Irons, C.J. Brindley and R. Bonn*
Huntingdon Research Centre Ltd., Huntingdon, UK; * Schwarz Pharma AG, Monheim, FRG.

1A2 Preliminary pharmacokinetic data on the irreversible aromatase inhibitor FCE 24304 in postmenopausal women.
Pianezzola E., **M. Breda**, R.C. Coombes*, M. Strolin Benedetti, M. Lassus and E. di Salle
Farmitalia Carlo Erba, R&D - Erbamont Group, Milan, Italy; * St. George's Hospital, London, UK.

1A12 Individualization of therapy - the problem of sustained carbamazepine preparation.
Plavsic Franjo, Gordana Prevodan and **Tanja Alebic-Kolbah***
Rebro Hospital Center, Zagreb, Yugoslavia.

1A11 Investigation on a possible induction of AZT glucuronidation by rifabutin and rifampicin in humans.
Strolin Benedetti M., P. Duchene* and P. Olliaro
Farmitalia Carlo Erba, R&D - Erbamont Group, Milan, Italy and * ADME Bioanalyses, Mougins, France.

1A1 Pharmacokinetics and metabolism of diltiazem in healthy volunteers following a single oral dose.
Yeung Pollen K.F., Chris Prescott, Camille Haddad, Dorothy Marshall, Helen Tremayne, Carl McGregor, Michael A. Quilliam* and Terrence J. Montague
College of Pharmacy and Division of Cardiology, Dalhousie University and Victoria General Hospital, Halifax, Nova Scotia, Canada B3H 3J5; * Institute of Marine Biosciences, National Research Council, Halifax, Nova Scotia, Canada.

1A16 The use of earlobe blood sample in studies on the pharmacokinetics of digoxin.
Zhou Jia-Xiu and Ying Li
Pharmacy Laboratory, Lanzhou Airforce Hospital, 730070 Lanzhou, Gansu, P.R. China.

1A15 Studies on the pharmacokinetics with earlobe blood sample.
Zhou Jia-Xiu, Zhi-An Zheng, Yang Li and Jie Sheng
Pharmacy Laboratory, Lanzhou Airforce Hospital, 730070 Lanzhou, Gansu, P.R. China.